

HUMAN INFLUENZA A H5N1 (Pre-pandemic/Provisional)

✓ DISEASE AND EPIDEMIOLOGY

Clinical Description:

The reported symptoms of human illness caused by avian influenza viruses have ranged from typical influenza-like symptoms (e.g., fever, cough, sore throat, and muscle aches) to eye infections (conjunctivitis), pneumonia, acute respiratory distress, viral pneumonia, and other severe and life-threatening complications.

Causative Agent:

Influenza is an RNA virus. There are three types of influenza viruses, A, B, and C. Influenza B circulates only in humans, and Influenza C does not appear to cause epidemics. Influenza A viruses have a broad host range including birds, pigs, and humans. Influenza A viruses are subtyped based upon the structure of the hemagglutinin and neuraminidase proteins.

Avian influenza refers to those subtypes of Influenza A virus which typically circulate in birds rather than in humans. Examples include those with H5 or H7 proteins. Currently, Influenza A (H5N1) is circulating in Asia and parts of Eastern Europe, primarily in bird populations.

Differential Diagnosis:

It is difficult to distinguish influenza A and B, and parainfluenza clinically.

Laboratory identification:

Most rapid tests are capable of identifying most strains of avian influenza. However, a negative rapid test should not preclude further testing in an individual with clinical symptoms and a relevant exposure to birds/human cases within the correct incubation period. Samples from individuals who are suspected of having avian influenza should not be sent to a laboratory for culture.

UPHL: At this time, the Utah Public Health Laboratory is the only laboratory in Utah capable of identifying influenza A (H5N1). Identification is through PCR that will type the isolate as influenza A or B, and further subtype influenza A as H1, H3, H5, or H7.

Treatment:

The following influenza treatment guideline is for human influenza. Treatment of avian influenza infections of humans is not a well-established area and advice of an expert should be sought. UDOH is prepared to assist in obtaining expert advice.

At this time, evidence suggests that oseltamivir (Tamiflu), and probably zanamivir (Relenza), will have some efficacy as a treatment for the avian influenza (H5N1)

circulating currently in Asia. However, at least one isolate has been reported that appeared to be resistant to oseltamivir.

Information on dosage and routes of administration can be found at:

<http://www.cdc.gov/flu/professionals/treatment/index.htm>

	Rx Adult	Rx Child	Prophy Adult	Prophy Child
Amantadine (Symmetrel)	Yes (Type A only)	Ages > 1 year (Type A only)	Yes (Type A only)	Ages > 1 year (Type A only)
Rimantadine (Flumadine)	Yes (Type A only)	Not licensed	Yes (Type A only)	Ages > 1 year (Type A only)
Oseltamivir (Tamiflu)	Yes	Ages > 1 year	Yes	Ages >1 years
Zanamivir (Relenza)	Yes	Ages > 7 years	Not licensed	Not licensed

CDC encourages the use of

- **amantadine or rimantadine for chemoprophylaxis** and
- **use of oseltamivir or zanamivir for treatment**

as supplies and susceptibilities allow, in part minimizing the development of amantadine resistance among circulating influenza viruses.

To reduce the emergence of antiviral drug-resistant viruses, amantadine or rimantadine therapy for persons with influenza A illness should be discontinued as soon as clinically warranted, typically after 3–5 days of treatment or within 24–48 hours after the disappearance of signs and symptoms. The recommended duration of treatment with either zanamivir or oseltamivir is 5 days.

Treatment of influenza with antivirals should start as soon as possible, but within 48 hours of disease onset for maximum reduction in symptom severity and duration.

Case fatality:

The case fatality rate of influenza A (H5N1) as acquired by humans is as yet unknown as large studies, designed to look for subacute cases, have not yet been published. For hospitalized cases, mortality appears to be approximately 60%.

Reservoir:

The virus has been identified in a number of avian and other species, but the greatest human risk has come from domesticated chicken, ducks, and turkeys.

Transmission:

Infected birds shed influenza virus in their saliva, nasal secretions, and feces. Susceptible birds become infected when they have contact with contaminated excretions or surfaces that are contaminated with excretions. It is believed that most cases of bird flu infection in humans have resulted from contact with infected poultry or contaminated surfaces.

Notable findings of epidemiologic investigations of human H5N1 cases in Vietnam during 2005 have suggested transmission of H5N1 viruses to at least two persons through consumption of uncooked duck blood. There is no evidence that any human cases of avian influenza have been acquired by eating cooked poultry products.

So far, no sustained human-to-human transmission of the H5N1 virus has been identified, and no evidence for genetic reassortment between human and avian influenza A virus genes has been found; however, the epizootic in Asia continues to pose an important public health threat.

Susceptibility:

At this time, susceptibility to severe disease with avian influenza has not been well defined. With influenza A and B (human strains), children under 2, adults over 65, and individuals with certain chronic illnesses tend to have more severe illness/sequelae than healthy individuals between 5 and 49 years of age. Avian influenza infections of humans in this current epizootic have often affected children and young adults. It is not clear whether this is related to exposure or susceptibility.

Incubation period:

The incubation period for human influenza ranges from 1-4 days with an average of 2 days. For purposes of surveillance, providers are encouraged to look for avian influenza if the patients have had appropriate exposure risk within 10 days of onset of symptoms.

Period of communicability:

Influenza patients (with typical human strains of influenza) can shed virus from 1 day prior to onset of symptoms until 3-5 days after onset, but can be transmitted up to 7 days after symptom onset in children. Immunocompromised persons can shed virus for weeks to months after infection.

Epidemiology:

Research suggests that currently circulating strains of H5N1 viruses are becoming more capable of causing disease (pathogenic) in mammals than were earlier H5N1 viruses. H5N1 viruses are becoming more widespread in birds in the affected regions. One study found that ducks infected with H5N1 virus are now shedding virus for longer periods without showing symptoms of illness. This finding has implications for the role of ducks in transmitting disease to other birds and possibly to humans as well. Additionally, other findings have documented H5N1 infection among pigs in China and H5N1 infection in felines (experimental infection in housecats in the Netherlands and isolation of H5N1 viruses in tigers and leopards in Thailand), suggesting that cats might host or transmit the infection. Currently, there is evidence that migratory birds may carry the virus for long distances, infecting local poultry flocks with the virus.

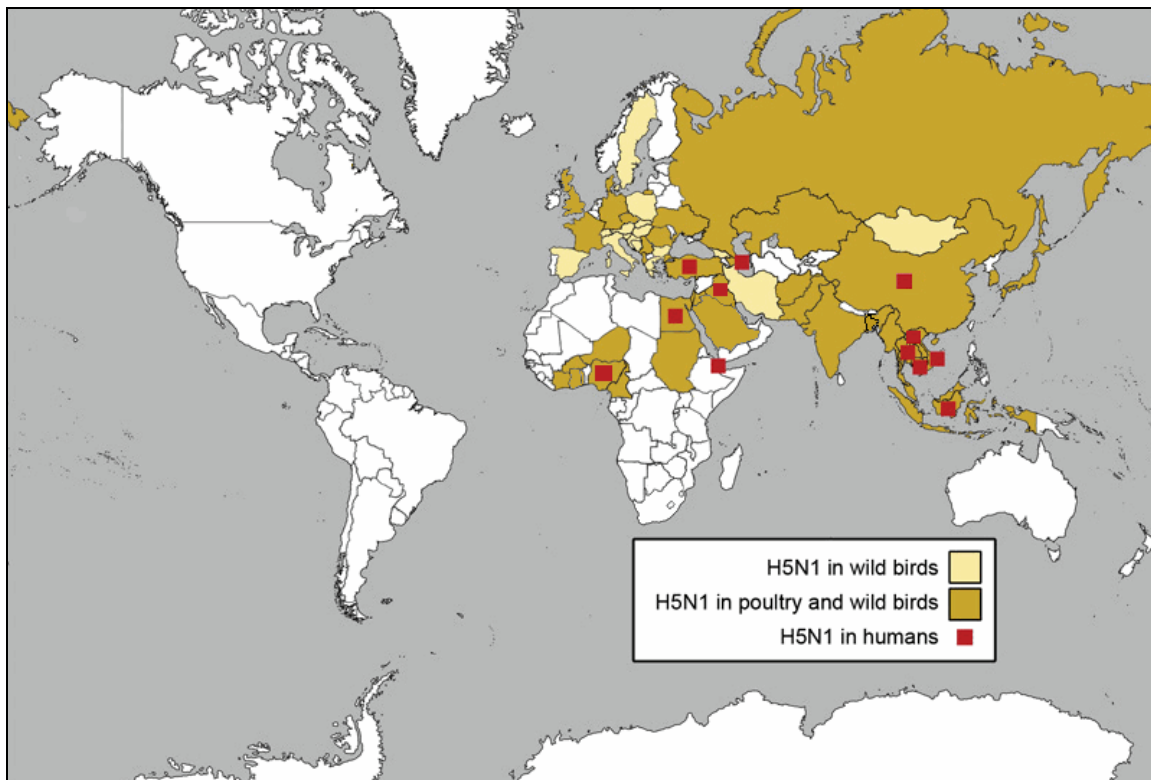


Image Courtesy CDC

✓ PUBLIC HEALTH CONTROL MEASURES

Public health responsibility:

- The primary public health responsibility for avian influenza is to rapidly identify individuals infected with this variant form of influenza and prevent or limit further spread of the infection.
- Public health should also provide education to clinicians and the general public about avian influenza and provide timely updates about the current situation.
- Public health also has responsibility for developing plans to respond to a human outbreak of a novel influenza virus, often called a pandemic. That responsibility, “pandemic influenza planning,” is not systematically addressed in this document which applies to the current situation where avian influenza is circulating as an epizootic in other parts of the world than Utah and has not demonstrated effective person-to-person transmission.

Prevention:

Influenza viruses such as H5N2, H7N2, and H5N1 are destroyed by adequate heat, as are other foodborne pathogens. Consumers are reminded to follow proper food preparation and handling practices, including:

- Cook all poultry and poultry products (including eggs) thoroughly before eating. (This means that chicken should be cooked until it reaches a temperature of 180 degrees Fahrenheit, throughout each piece of chicken.)

- Raw poultry always should be handled hygienically because it can be associated with many infections, including salmonella. Therefore, all utensils and surfaces (including hands) that come in contact with raw poultry should be cleaned carefully with water and soap immediately afterwards.

The World Health Organization has developed food safety guidance for the current situation in Asia. This is available at <http://www.who.int/foodsafety/micro/avian/en/>.

Traveler Health:

<http://www.cdc.gov/travel/seasia.htm>

Vaccine:

Efforts to produce vaccine candidates that would be effective against avian influenza A (H5N1) virus are under way. Currently, no licensed human vaccine for Influenza A (H5N1) exists.

Isolation and quarantine requirements:

Special precautions need to be taken with cases of avian influenza to limit the potential for transmission to other humans. While sustained person-to-person transmission of avian influenza has not been observed at the time this document was prepared, there is a risk that the virus could become capable of such transmission either by direct adaptation in humans or other animals or through viral reassortment that would mix the pathogenic genes of the avian influenza with the readily transmissible human influenza strains. Therefore, it is considered prudent to take all possible precautions, to the extent feasible, when caring for patients with known or possible avian influenza.

Human influenza is transmitted primarily via large droplets (respiratory). Therefore, Standard and Droplet Precautions have been recommended for human influenza. Because exact transmission patterns are not yet well defined for avian influenza, as well as the risk of serious disease and increased mortality, additional precautions are prudent.

Clinician offices (for all respiratory disease):

- Inform all patients upon entrance into your facility of the importance of notifying reception staff of respiratory symptoms (cough with fever or rash).
- Educate patients on the importance of respiratory etiquette (covering cough, washing hands)
- Consider putting a procedure or surgical mask (N-95 is not required) on patients with respiratory symptoms.
- Clinic personnel should follow droplet precautions (wear a procedure or surgical mask) when examining a patient with respiratory symptoms (especially those with a fever or rash in addition to a cough).
- Request a history of travel within 10 days of disease onset. If patient visited a country with history of avian influenza in poultry AND had close contact with birds/poultry or consumed/touched raw poultry products, notify public health immediately.

Management of patients with or under evaluation for avian influenza (healthcare setting):

- Standard Precautions (careful hand hygiene before and after all patient contact or contact with items potentially contaminated with respiratory secretions).
- Contact Precautions (gloves and gowns for all patient contact, dedicated equipment such as stethoscopes, disposable blood pressure cuffs, disposable thermometers, etc.)
- Droplet Protection (all people entering the room should wear a NIOSH-approved fit-tested disposable respiratory (at least N-95) when entering the room)
- Airborne Precautions (place patient in airborne isolation room).
Note: nebulizers and high-air flow oxygen masks have been implicated in nosocomial spread of other respiratory viruses and should be used only with strict airborne precautions. The ability of influenza to be transmitted via small droplets (e.g. airborne) is still unclear.
- Identification, surveillance, and monitoring of clinical personnel with respiratory exposure to patients.
- Consider pre- or post-exposure prophylaxis of exposed healthcare workers with oseltamivir for 7-10 days.

Management of patients with or under evaluation for avian influenza (home setting):

- Advise patient to stay home (with the exception of visiting a health-care provider) until diagnostic testing is negative for avian influenza.
- Educate patient on respiratory etiquette.
- Household members should not share utensils, avoid face-to-face contact with suspect/confirmed cases, and consider wearing masks and eye protection.
- Household members should also consider monitoring their temperature twice daily and monitoring for symptoms for 7 days following the last exposure.
- If household members develop fever ($>38^{\circ}\text{C}$), cough, diarrhea, shortness of breath, or other systemic symptoms, consider antiviral therapy as soon as symptoms begin.

Quarantine of patients with exposure to known avian influenza or isolation of individuals with known avian influenza infection:

- First, assure that the above precautions (standard, contact, eye, and airborne) are enacted.
- Next, possible quarantine actions should be discussed with the State Epidemiologist prior to enacting.

Surveillance and monitoring of exposed healthcare workers:

- Instruct healthcare workers who were exposed to known cases of avian influenza-infected patients, to watch for the development of fever, respiratory symptoms, and/or conjunctivitis (eye infections) for 7 days after their last exposure. If they become ill (for any reason), they should seek medical care and, prior to arrival, notify their provider that they were exposed to avian influenza. Also, employees should notify occupational health and infection control personnel at their facility.

All exposed healthcare workers who are ill (for any reason) should not be involved in any direct patient care.

- Ideally, all exposed healthcare workers should monitor their temperature twice daily and report any febrile event.
- The request to notify health care provider before coming in applies to others who had potential poultry exposure in the affected countries as well as to health care providers.

✓ CASE INVESTIGATION

Reporting:

All suspect cases of influenza A (H5N1) are reportable to public health.

Case definition:

Avian Influenza Surveillance Criteria:

A patient who has an illness that:

- Requires hospitalization or is fatal... AND
- Has or had a documented temperature of $>38^{\circ}\text{C}$ ($>100.4^{\circ}\text{F}$)... AND
- Has radiographically-confirmed pneumonia, ARDS, or other severe respiratory illness for which an alternate diagnosis has not been established... AND
- Has at least one of the following potential exposures within 10 days of symptom onset:
 - History of travel to a country with influenza H5N1 documented in poultry, wild birds, and/or humans (see www.who.int for current list) AND at least one of the following potential exposures during travel:
 - Direct contact with (e.g. touching) sick or dead domestic poultry
 - Direct contact with surfaces contaminated with poultry feces
 - Consumption of raw or incompletely cooked poultry or poultry products
 - Direct contact with sick or dead wild birds suspected or confirmed to have influenza H5N1.. OR
 - Close contact (within 3 feet) of a person who was hospitalized or died due to a severe unexplained respiratory illness
 - Close contact (within 3 feet) to an ill patient who was confirmed or suspected to have H5N1....OR
 - Worked with live H5N1 virus in a laboratory

Testing in situations that do not meet the above criteria can be considered on a case-by-case basis, in consultation with the Utah Department of Health Bureau of Epidemiology and the Utah Public Health Laboratory.

Procedure for Ruling out Avian Influenza:

- Patient should meet the above surveillance criteria in order to request testing from UPHL.
- Obtain a listing of symptoms. Avian influenza is a febrile respiratory illness, and patients should have symptoms compatible with this syndrome.
- Obtain the date of onset of first symptoms.

- Request a detailed exposure history, including all out-of-country travel, dates of travel, and type of exposure to live poultry or raw poultry products.
- Contact the Local Health Department or UDOH Bureau of Epidemiology if patients have compatible symptoms and exposure history. Local health department personnel should contact the Bureau of Epidemiology.
- Assure that both a nasopharyngeal and an oropharyngeal swab from the patient (assure that medical personnel follow standard, droplet, and contact precautions while collecting the specimen. If patient is hospitalized, add airborne precautions.). Also collect a serum sample in a red top or serum separator tube.
- Fax or email the test request form to the clinician, which should be filled out and submitted with the sample.
- Place the NP and OP swabs into individual tubes of M4 (viral culture) media. Assure transport as soon as possible at 4 degrees C (wet ice) to the Utah Public Health Laboratory. ***Note: do NOT send samples for culture.***
- The respiratory sample will be tested by RT-PCR for influenza A and B and for the subtypes of influenza A including H1, H3, H5, and H7.
- ***Note: Do NOT send the sample to a commercial laboratory for viral isolation unless the facility is pre-notified and is capable of viral culture in 3+ biosafety level.***

Case Investigation Process:

During the testing phase, the patient should be isolated, either in a hospital isolation room or at home. Their contact with other individuals should be minimized. Patients should be educated on appropriate respiratory etiquette.

Outbreaks:

There have been no outbreaks of avian influenza in humans due to sustained human-to-human transmission of avian influenza (H5N1).

Identification of case contacts and management:

Isolation is not required for exposed contacts. In the event that a suspect case was confirmed as being H5N1 influenza, a conference call would be held and additional information would be forthcoming at that time.

REFERENCES

The World Health Organization Global Influenza Program Surveillance Network;
Evolution of H5N1 Avian Influenza Viruses in Asia; Emerg Infect Dis.
2005;11(8) ©2005 Centers for Disease Control and Prevention (CDC)

The Writing Committee of the WHO Consultation on Human Influenza A/H5; Avian Influenza A (H5N1) Infection in Humans; NEJM 353(13), 1374-1384, 2005.

CDC and WHO Web Sites